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New industry research and approaches that could help to improve the risk assessment on bees

February 2017

Conclusions of the EFSA journals since Jan 2016: Need an Alternative Approach

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Date and link to EFSA journal	Substance	Crops	Conclusions of EFSA	Data Gaps identified by EFSA	Higher Tier data EFSA acceptance
19 January EFSA Journal 2016;14(1):4374 [141 pp.].	Ethofumesate (herbicide)	*Sugar beet* *Fodder beet* *Red beet*	Do not pass the Bee Risk Assessment	Further information to address the risks in crop, from flowering weeds, in field margins, and in adjacent and succeeding crops Further information to address the risks from metabolites in nectar and pollen Further information to address the MRLs in honey	Rejected - Non EFSA compliant
19 February EFSA Journal 2016;14(3):4419 [103 pp.].	Mesotrione (herbicide)	*Maize*	Do not pass the Bee Risk Assessment	Further information to address the effects on HPG gland development Further information to address the acute and chronic risks to adults and larvae from guttation, and water consumption Further information to address the risks from metabolites in pollen and nectar	Not evaluated (no data available)
19 February EFSA Journal 2016;14(3):4421 [119 pp.].	Foramsulfuron (herbicide)	*Maize*	Do not pass the Bee Risk Assessment	Further information to address the risk to honeybees from sublethal effects (HPG) Further information to address the risks from consumption of contaminated water Further information to address the risks from metabolites in pollen	Rejected - Non EFSA compliant
22 February EFSA Journal 2016;14(2):4406 [171 pp.].	Fenamidone (fungicide)	*Potato* *tomato*	Do not pass the Bee Risk Assessment	Further information to address the effects on HPG development Further information to address the chronic risk in crop and from flowering weeds Further information to address the risk to larvae from flowering weeds and in succeeding crops and the residue intake with contaminated water Further information to address the risk from metabolites in pollen and nectar	Rejected - Non EFSA compliant
24 February EFSA Journal 2016;14(2):4416 [115 pp.].	Isoxaflutole (herbicide)	*Maize* *Sweet corn* *Soy bean*	Do not pass the Bee Risk Assessment	Further information to address the risks from metabolites in pollen	Rejected - Non EFSA compliant
17 March EFSA Journal 2016;14(3):4420 [212 pp.].	Pendimethalin (herbicide)	*Cereals* *Carrot* *Beans* *Peas* *Winter cereals*	Do not pass the Bee Risk Assessment	Further information to address the chronic risk to honeybees; Further information to address the risk of sublethal effects (i.e. HPG development effects) Further information to address the risk to honeybees due to plant metabolites occurring in pollen and nectar	Not evaluated (no data available)
1st April EFSA Journal 2016;14(4):4432 [116 pp.].	Imazamox (herbicide)	*Sunflower* *Alfalfa* *Soybean* *Winter OSR* *Spring OSR*	Do not pass the Bee Risk Assessment	Further information to address effects on HPG development Further information to address the risk of residue intake with contaminated water (guttation fluids and puddle) Further information to address the risk to the metabolites in pollen and nectar (this information is relevant for all representative uses evaluated	Not evaluated (no data available)
19 April	Iodosulfuron (herbicide)	*Winter Wheat* *Winter Barley*	Do not pass the Bee Risk Assessment	Further information to address the risk of sub-lethal effects (i.e. HPG development effects) Further information to address the risk to honeybees larvae due to exposure to contaminated water;	Rejected - Non EFSA compliant

Impact Analysis.zip

List of all 2016 conclusions

Outline

1. Data requirements vs Availability of Test Methods
2. Tier 1 Risk Assessment Honeybee
3. Tier 2 Risk Refinement Options
4. Higher tier studies and refinements Options
5. Field studies

Supporting data are available for each point of the industry proposal and available on request

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Data Requirements vs Availability of Test Methods

Available Testing methods

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Honeybees

- Full set of first tier testing methods and high tier testing methods are available for adults and larvae to be able to profile active substances

Bumble bees and solitary bees

- Draft methods being ring tested for acute bumble bees
- No chronic, larval or high tier testing method for bumble bees
- No method for solitary bees

Honey bees a surrogate for non-Apis bees

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- **On testing and sensitivity of non-Apis species**
  - Existing data reviews highlight honey bees are a good surrogate for non-Apis bees: Sensitivity of non-Apis bees within a factor of 5 or less of honeybees 90% of the time (Thompson, 2016).
  - It took <5 years to develop new methods for the honeybee, so new method development for non-Apis bees will not be available in short-medium term
  - Industry will continue to participate in ICPPR and OECD method development

- **Therefore need to focus risk assessment on honeybees, which is the more reliable and scientifically robust option currently**

- **The highly conservative exposure approaches used for individual honeybees to pollen and nectar should be protective for non-Apis bees (Guidance [Document] for Assessing Pesticide Risks to Bees [EPA, PMRA & CDPR, June 19, 2014])**

Testing of Formulations & Metabolites

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Focussed Testing of formulations

- Routine chronic and larval testing should not be required on every preparation
- Instead: Based on EFSA (2013):
  - Focus on acute testing (more appropriate to compare accurate estimates of intrinsic toxicity)
  - If the formulation is more toxic than the active substance (factor of 5) then additional testing would be triggered.

This would be better aligned with guidance documents worldwide and reduce pressure on available testing capacity.

Focussed Testing of metabolites

- Should be driven by an examination of existing data on other organisms, and biological screening
- Higher exposure of bees to parent will compensate for any higher toxicity of metabolite. Therefore the risk from metabolites will be covered by the parent in the vast majority of cases
- Testing should be focused only on insecticides and major plant metabolites, and major soil systemic metabolites
- Testing should focus on acute toxicity as a screening for further (chronic) testing, as for other areas of ecotoxicology

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Tier 1 risk assessment honeybees

Exposure routes

- **Focus on nectar and pollen: as main dietary exposure route**
  - Increasing published evidence of a lack of a colony level risk from exposure via guttation
  - There is no evidence of the relevance of puddles as a significant colony level exposure route

- **Succeeding crops should be only considered for highly persistent, highly toxic and highly systemic compounds**

- **Flowering weeds: a large industry data set available to show for arable crops flowering weeds will not trigger EFSA concern to consider this as a relevant route of exposure**
  - For perennial crops (orchards, vineyards) risk from flowering weeds can be managed with mitigation measures e.g. cutting/mulching weeds.

Tier 1 Risk Assessment Approach

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Acute Risk

- **Use SANCO 10329/2002**
  - Provides a comparable outcome (pass/fail rate) as EFSA (2013).
  - No need to amend the uniform principles
  - Recent publications revalidate this approach for sprayed products and acute risks
  - EPPO (2010) is still valid for sprayed products and systemic seed treatments.
- **Chronic Risk**
  - The ECPA impact analysis and results of recent EFSA evaluations confirm the excessive conservatism of the EFSA approach i.e. multiple failures even for products with no inherent bee toxicity.
  - There are 2 potential alternative options that could be developed to solve this problematic area: see Next Slide

Chronic Honeybee Risk Assessment Option 1

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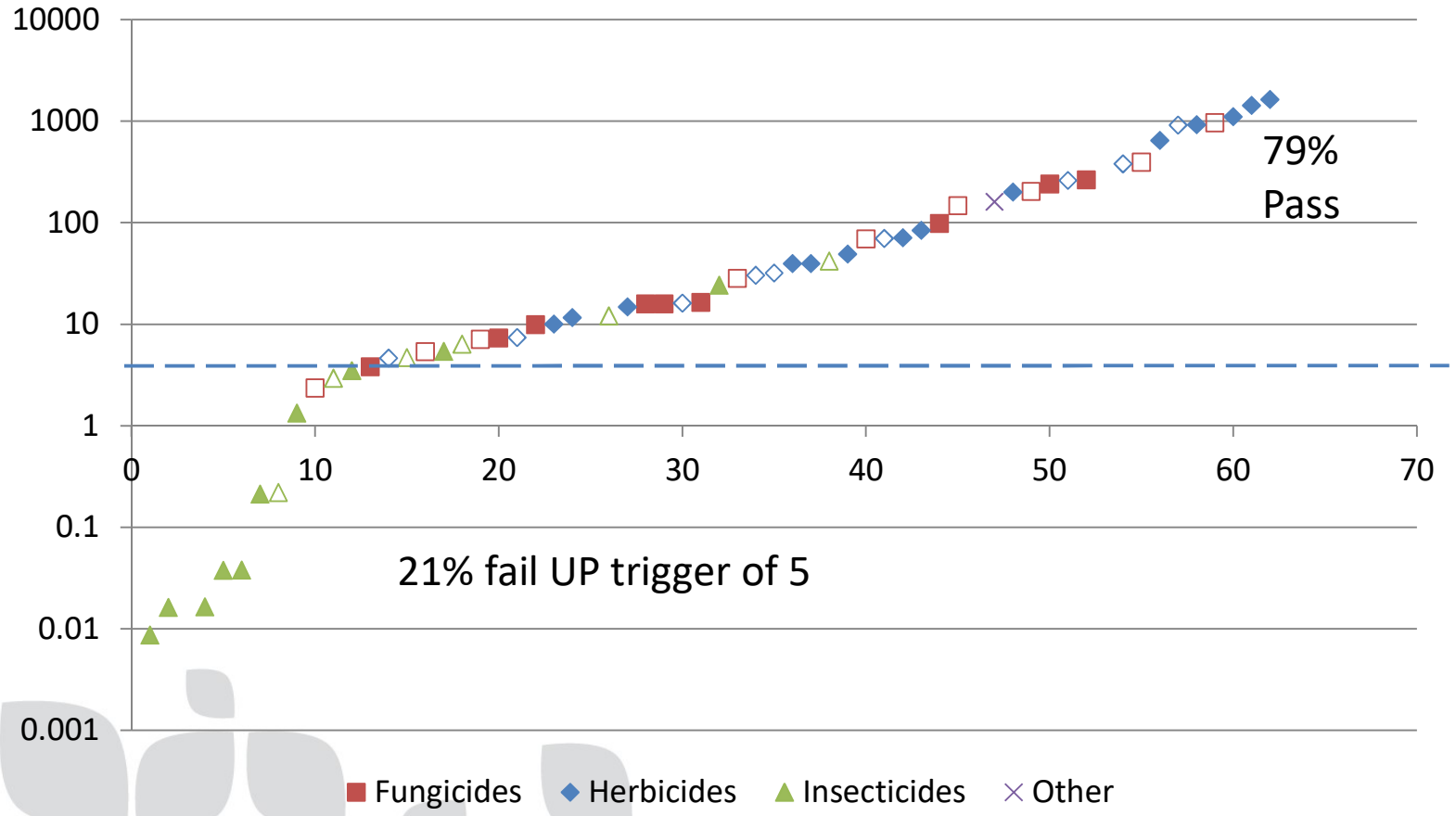
Use EPPO (2010) together with EFSA RUD and a more ecologically representative 30% sugar scenario (USEPA). Here with mean RUD, NOED and as an example trigger of 5 for illustrative purposes only



Hollow symbols indicate lack of effects at higher tier / direct overspray. Solid symbols indicate not tested/no data

Chronic Honeybee Risk Assessment Option 2

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Using EFSA approach to set quantitative protection goals

- Specific protection goal (SPG) set to max 7% reduction in colony size compared to control
- Khoury model used to translate increase in forager mortality to SPG as 1.27x in hive background mortality (5.3%) over 10 day
- Max. increment = 0.27*5.3 = 1.43 % (ie 1 dead bee in 68)
- Using linear interpolation chronic trigger set as

$$\frac{50\ \%}{1.43\%} = 34\ (0.03)$$

- Linear model over estimates trigger as true dose-responses are sigmoidal

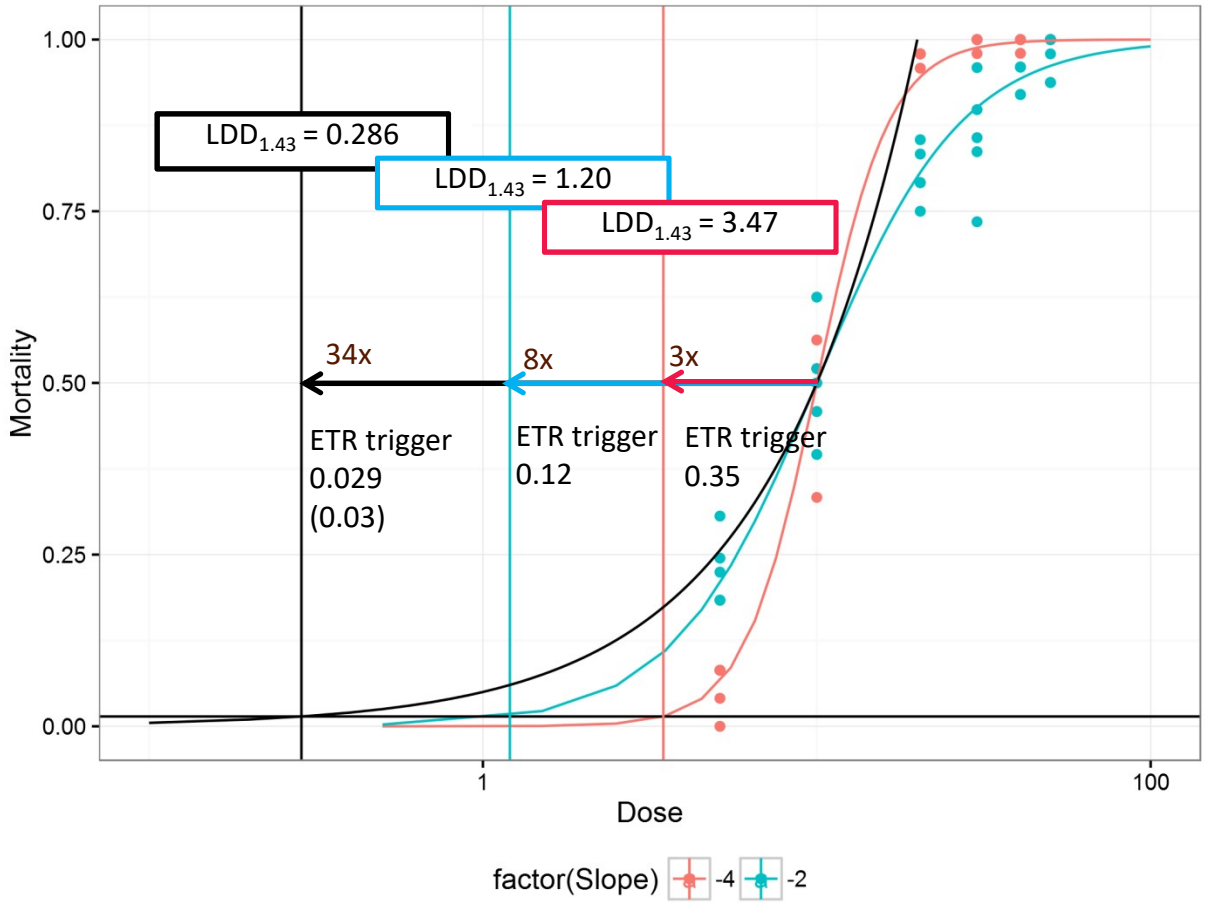
- Note: where NOEDD is used in place of LDD_{50} leads to further over estimation so needs revised trigger (assuming NOEDD = LDD10)

$$\frac{10\ \%}{1.43\%} = 6.99\ (0.143)$$

Chronic Honeybee Risk Assessment Option 2:

Simulated Example for different slopes and $LDD_{1.43}$

– each compound same LDD_{50} = 10 ug/bee/day



➔ different slopes give different $LDD_{1.43}$ at the same LDD_{50}

➔ EFSA assumption is $LDD_{1.43}$ is 34x smaller than LDD_{50}

Tier 1 Larvae Risk Assessment

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– **The risk assessment based on EFSA (2013) does not discriminate between toxic and non toxic compounds**

  - This is driven by exposure assumptions that are much higher than in real life (e.g. residues in unprocessed food, no dilution in the hive).
  - Experimental data on residues in larvae and royal jelly as well as modelling are now available to confirm the low level of exposure of larvae to residues
    - For example, the use of a median RUD would be a minimum!

Option 1

Use EPPO (2010) together with EFSA RUD and 30% sugar (ecologically relevant scenario) with mean RUD, NOED and trigger of X (as for the adults before)

Option 2

Use concentrations in the risk assessment equation and in measuring the endpoint

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Tier 2 Risk Refinement Options

Exposure refinement:
Residue (bee exposure) study Options

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- **Industry data available in the biology efficacy section can be used to define an application rate that may confirm a lower uncertainty than expected regarding residue levels.**
  - i.e. if applications are rather consistent in effect on the target organism variability is therefore low indicating that 5 trials per region should not be required to reach the 90th percentile
- **The analysis of these new industry biological data as well as industry residue trials could also help with the definition of crop groups within which residue levels are expected to be similar**
- **The development of standards for residue studies performance as a function of environmental factors that influence residue content would be a basis towards a further guidance**

Exposure refinement: New Modelling Approaches

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- **Allows to generate worst case exposure scenarios, using observed biology traits as a basis**
- **BEEHAVE model available**
  - Ongoing development of worst case realistic exposure scenarios to be used in Tier 1 and Tier 2
  - Pesticide module in final development phase
- **Modelling is an alternative to costly field exposure studies and can be used to test many more scenarios than experiments, and cover uncertainties relative to geographical differences, agricultural practices etc.**
- **The potentialities of modelling could be further explored in a dedicated working group to accelerate the development of the scenarios mentioned above**

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Higher tier studies and Risk Refinement Options:

Higher tier options for risk assessment

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- **Risk to adult bees at tier 1:**
  - Refine exposure with residues if possible (experimentation or modelling)
  - EPPO 170 tunnel test, 7-day exposure, and monitor colonies over up to 2 brood cycles, 4-5 replicates per dose, 20 tunnels in total (number of replicates being practicable) and include exposure verification.

- **Risk to brood at tier 1:**
  - Refine exposure with residues if possible (experimentation or modelling)
  - OECD 75: Although significant issues due to confinement of colonies in tunnels.
  - Oomen study, which can deal with concentrations and allow for adaptable feeding periods and can be linked to residue and modelling

Field studies Options

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- **Modify existing EPPO 170 Field Study Guidance – ICP-PR Working Group**
  - Field studies should be designed to address specific problem formulation
  - Ideally they would be replicated and allow for statistical evaluation, e.g. Rundlof 2015 Honeybee Field Study.
  - Several scientific papers have been suggested that would be worth reviewing to improve existing protocols

- **Possible Alternative to field studies: Colony feeding studies**
  - Allow to control the level of exposure
  - Link to residue studies
  - Interpretation can be facilitated by the BEEHAVE model
  - Alternative to full field trial, in which parameters are better controlled than in a field trial
  - Protocol to be designed by ICP-PR based on current EPA methodology

Conclusions

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- **The EFSA document is not practical and cannot be used without major revisions**
  - In its current form, it is generating a number of uncertainties and data gaps in the conclusions of risk assessments, as observed in the EFSA journals on active substances published since January 2016
- **The current situation is unsustainable for all parties. A new way forward is needed**
- **New data and approaches proposed in this presentation summarize the outcome of over 3 years of research to propose a protective and alternative way forward which could be developed further with Member State & EFSA Experts**
  - It includes the outcome of collaboration with expert groups during workshops, as well as experience in method development
  - Supportive information is available on request
- **Industry is committed to pursue dialog with regulatory authorities and EFSA to share our experience and data to help develop a workable way forward**